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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
BELYAVSKYI, MICHAIL A	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 02/23/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/986,897	PELED ET AL.	
	Examiner	Art Unit	
	Michail A Belyavskyi	1644	

-- The MAILING DATE of this c mmunication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 December 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5,7,8,18-23,25-30,32-34,36,42-48 and 51-62* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5,7,8,18-23,25-30,32-34,36,42-48 and 51-62* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

RESPONSE TO APPLICANT'S AMENDMENT

1. Applicant's amendment, filed 12/02/03 is acknowledged.

Claims 1-5, 7-8, 18-23, 25-30, 32-34, 36, 42-48 and 51-62 are pending.

Claims 1-5, 7-8, 18-23, 25-30, 32-34, 36, 42-48 and 51-62 as they all read on the elected expanded hematopoietic cell population wherein neonatal umbilical cord blood is species of specific hematopoietic cells , tetraethylenepentamine (TEPA) is specific transition metal chelator, FLT3 and G-CSF is specific early and late acting cytokine are under consideration in the instant application.

2. Applicant's amendment filed 12/02/03 and declaration of Dr. Eitan Fibach under 37 CFR 1.132 have obviated the previous rejections of record mailed on 6/2/03.

3. The following new grounds of rejection are necessitated by the amendment filed 12/02/03.

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 1-5, 7-8, 18-23 and 51-56 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **This is a New Matter rejection.**

" ...cell population of committed progenitor hematopoietic cells and/or non-differentiated, early hematopoietic progenitor cells" claimed in claim 1 represent a departure from the specification and the claims as originally filed. The passages pointed by the applicant do not provide a clear support for specific subgenus of committed progenitor hematopoietic cells and/or non-differentiated, early hematopoietic progenitor cells.

The specification and the claims as originally field only support a genus of " hematopoietic cells and progenitor cells". See *In re Smith* 173 USPQ 679, where it was ruled that a genus may not support a subgenus even though there is a disclosed species within the subgenus.

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

7. Claims 1-5, 7-8, 18-23, 25-30, 32-34, 36, 42-48 and 51-62 are rejected under 35 U.S.C. 103(a) as being unpatentable over Moore et al(Blood Cells, 1994, v.20, pages 468-481) or C.De Bruyn et al., (Stem Cells 1995, v.13, pages 281-288) each in view of Cicuttine et al (Blood, 1992, v 80, pp 102-112) and of Percival et al (J Nutrition, 1992, v122 pages 2424-2429).

Moore et al. teach an hematopoietic cell population comprising obtaining hematopoietic cells from a donor, ex-vivo expansion of said cells and transplanting said cells to a patient (see, entire document, abstract in particular). Moore et al. teach that the hematopoietic stem cells can be derived from umbilical cord blood (see page 469 in particular). Moore et al. teach a growth medium with nutrients and early and late acting cytokines (See Material and Methods in particular). Moore et al. teach that ex vivo expansion of cord blood CD34+/CD38- cells will permit improved engraftment of adults (see abstract in particular).

Similarly, C.De Bruyn et al. teach an hematopoietic cell population comprising obtaining $CD34^+$ hematopoietic cells from a donor, ex-vivo expansion of said cells and transplanting said cells to a patient (see, entire document, abstract in particular) C.De Bruyn et al. teach that the hematopoietic stem cells can be derived from umbilical cord blood or from bone marrow (see

Page 282, in particular). Moore et al. teach a growth medium with nutrients and early and late acting cytokines (See Material and Methods in particular).

Moore et al. or C.De Bruyn et al. does not explicitly teach an expanded hematopoietic cell population obtained by ex-vivo culturing under define growth conditions for cell proliferation and in the presence of a transition metal chelator , such as TEPA having an affinity for copper wherein said chelator inhibits differentiation of said cells while permitting expansion.

Cicuttine et al. teach culturing hematopietic stem or progenitor cells using define growth condition that will stimulate growth while inhibit differentiation (see entire document, page 104, column 2 in particular). Cicuttine et al. teach isolating bone marrow cells from adults using methods known in the art (see page 103 in particular). The growth media containing nutrients, early and late acting cytokines (including G-CSF) and zinc, a transition metal chelator having an affinity for copper. Cicuttine et al. teach that zinc has an affinity to copper and would reduce copper utilization of culturing hematopoietic cells (see Discussion in particular). Therefore cells culturing the in the medium containing zinc would obviously reduces a capacity in utilizing cooper. Cicuttini et al. teach a cell population isolated from the growth medium and resuspended in PBS that is considered to be a pharmaceutical composition comprising the cells. (see Materials and Methods, page 103 in particular)

Percival et al. teach culturing HL-60 cells in define growth medium condition that will stimulate growth while inhibit differentiation. (see entire document, Abstract in particular). It is noted that HL-60 cells are hematopoietic cells because they are myeloblastic and promyelocytic lymphoid cells which are hematopoietic cells. Percival et al. teach that cells can be made copper deficient by incubating them in the media containing tetraethylenepentamine (TEPA), TEPA and zinc or TEPA and copper (see Abstact and Material and Methods in particular) . Percival et al. teach that copper is essential for the process of differentiation and chelating copper with tetraethylenepentamine will inhibit differentiation (see page 2428 in particular). Percival et al. teach that growth rate of HL-60 was not affected by TEPA , while TEPA did not allow differentiation. (see abstract in particular). Percival et al , stated that " if copper is essential for differentiation then chelation of copper with TEPA should prevent the cell from differentiation" (see Applicant argument filed 12/09/03 page 12 in particular). Clearly one skill in the art would be aware of the fact that a transition metal chelator TEPA might be used to inhibit differentiation. Percival et al. teach a cell population isolated from the growth medium and resuspended in PBS that is considered to be a pharmaceutical composition comprising the cells. (see Materials and Methods, page 2425 in particular).

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to apply the teaching of Cicuttine et al. and Percival et al. and to those of Moore et al. or C.De Bruyn et al. to obtain a claimed an expanded hematopoietic cell population obtained by ex-vivo culturing under define growth conditions for cell proliferation and in the presence of a transition metal chelator , such as TEPA having an affinity for copper wherein said chelator inhibits differentiation of said cells while permitting expansion.

One of ordinary skill in the art at the time the invention was made would have been motivated to do so, because cultivating cells under growth conditions for reducing a capacity in utilizing copper using zinc containing medium or using a TEPA as a transition metal chelator having an affinity for copper will support only growth, proliferation and expansion without inducing differentiation of said cells will support only growth, proliferation and expansion without inducing differentiation of said cells as taught by as taught by Cicuttine et al. and Percival et al. that can be further used for ex-vivo expansion of hematopoietic cells and transplanting said cells to a patient as taught by Moore et al. or C.De Bruyn et al. The strongest rationale for combining references is a recognition, expressly or impliedly in the prior art or drawn from a convincing line of reasoning based on established scientific principles or legal precedent, that some advantage or expected beneficial result would have been produced by their combination. In re Semaker. 217 USPQ 1, 5 - 6 (Fed. Cir. 1983). See MPEP 2144.

From the combined teaching of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Claim 52 -54 and 58-60 are included because the claimed dosage of transition metal chelator from about 0.1 μM to about 100mM, or from about 4 μM to about 50 mM, from about 5 μM to about 40 mM overlaps the referenced 50 μM of TEPA and is therefore an obvious variation of the reference teaching absent a showing of unobvious property. Claims 55, 56, 61 and 62 are included because it would be conventional and within the skill of the art to identify the specific early and late acting cytokines to be used for ex-vivo culturing absent a showing of unobvious property. Further, it has been held that where the general conditions of a claim are disclosed in the prior art, discovering the optimum or workable ranges involves only routine skill in the art. *In re Aller*, 220 F2d 454,456,105 USPQ 233; 235 (CCPA 1955). see MPEP § 2144.05 part II A.

8. No claim is allowed

9. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michail Belyavskyi whose telephone number is 571/ 272-0840 The examiner can normally be reached Monday through Friday from 9:00 AM to 5:30 PM. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 571/ 272-0841 .

The fax number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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